I. AMENDMENT

In the Claims:

Please cancel claims 36, 37, 39, 41, 43-62 and 69-77 without prejudice or disclaimer.

Please amend claims 1, 3, 6, 12, 14-20, 25-29, 31-33, 35, and 67-68 as indicated below:

1. (Amended) A recombinant construct comprising:

(a) a DNA sequence encoding a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity, and

(b) a DNA sequence encoding a polypeptide having squalene epoxidase enzyme activity.

A1

3. (Amended) The recombinant construct of claim 1, further comprising a first promoter operably linked to said DNA sequence encoding a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity and a second promoter operably linked to said DNA sequence encoding squalene epoxidase enzyme activity, wherein said first and second promoters may or may not be the same.

A2

6. (Amended) A recombinant vector comprising operably linked in the 5' to 3' direction,

a promoter, a DNA sequence encoding a polypeptide having a 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity, and a transcription termination signal sequence;

a promoter, a DNA sequence encoding squalene epoxidase enzyme activity, and a transcription termination signal sequence.

A3

12. (Amended) A transformed host cell comprising a plant expression vector comprising,

(a) as operably linked components in the 5' to 3' direction, a promoter, a DNA sequence encoding a polypeptide having a 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity, and a transcription termination signal sequence; and

(b) as operably linked components in the 5' to 3' direction, a promoter, a DNA sequence encoding squalene epoxidase enzyme activity, and a transcription termination signal sequence.

A4

A5

14. (Amended) A cell culture comprising transformed host cells according to any one of claims 8-13.

15. (Amended) A transformed plant comprising at least one transformed host cell of any one of claims 8-13.

16. A plant according to claim 15 wherein said transformed host cell comprises a plant cell.

17. (Amended) A transformed storage organ, comprising at least one transformed host cell according to any one of claims 8-13.

18. (Amended) A transformed storage organ including at least one transformed host cell containing a recombinant vector comprising:

> (a) As operably linked components in the 5' to 3' direction, a promoter, a DNA sequence encoding at least one polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity, and a transcription termination signal sequence; and
>
> (b) as operably linked components in the 5' to 3' direction, a promoter, a DNA sequence encoding a polypeptide having squalene epoxidase activity, and a transcription termination signal sequence.

a5 cont

19. (Amended) The transformed storage organ according to claim 18 wherein said recombinant vector is a plant expression vector.

20. (Amended) A process of increasing the formation of steroid pathway products in a transformed host cell as compared to an otherwise identical non-transformed host cell comprising:

> (1) transforming a host cell with a recombinant vector comprising
>
> > (a) as operably linked components in the 5' to 3' direction, a promoter, a DNA sequence encoding a first polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity, and a transcription termination signal sequence; and
> >
> > (b) as operably linked components in the 5' to 3' direction, a promoter, a DNA sequence encoding at least one polypeptide having squalene epoxidase enzyme activity, and a transcription termination signal sequence, and
>
> (2) regenerating a transformed host cell into said transgenic plant.

a6

25. (Amended) A transgenic plant seed transformed with a vector comprising a DNA segment that encodes a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase activity, and a DNA segment that encodes a polypeptide having squalene epoxidase enzyme activity, and a promoter suitable for driving expression of said polypeptides in said plant cell, wherein said transgenic plant seed is capable of germinating into a transgenic plant that over-accumulates steroid pathway products relative to a non-transformed plant of the same species; and mutants, recombinants, genetically engineered derivatives thereof and hybrids derived therefrom, wherein said mutants, recombinants, genetically engineered derivatives thereof and hybrids derived therefrom maintain the ability to overaccumulate steroid pathway products.

26. (Amended) A plant, the genome of which includes introduced DNA comprising:

DNA encoding a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity, wherein said plant contains an elevated level of total accumulated sterol, compared to an otherwise identical plant, the genome of which does not comprise said introduced DNA encoding a polypeptide encoding 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity; and

further comprising introduced DNA encoding at least one polypeptide having squalene epoxidase enzyme activity,

wherein said introduced DNAs are operatively linked to regulatory signals that cause seed-specific expression of said introduced DNAs, and wherein seeds of said plant contain a reduced level of squalene, cycloartenol, 24-methylene cycloartenol, obtusifoliol, stigmasa-7-enol, or campestral compared to the seeds of an otherwise identical plant whose genome does not contain introduced DNA encoding said at least one polypeptide having squalene epoxidase enzyme activity.

27. (Amended) A plant, the genome of which includes an introduced DNA sequence encoding a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase activity and an introduced DNA sequence encoding at least one polypeptide having squalene epoxidase enzyme activity, wherein said introduced DNA is operably linked to regulatory signals that cause seed-specific expression of said introduced DNA, and wherein said plant produces seed having an elevated level of a steroid pathway product, compared to a corresponding transgenic or non-transgenic plant that does not contain said introduced DNA.

a6 concl

28. (Amended) A plant comprising introduced DNA encoding (i) a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity and (ii) at least one additional polypeptide having squalene epoxidase enzyme activity, wherein said plant that produces a storage organ having an elevated level of a sterol pathway product compared to a corresponding transgenic or non-transgenic plant that does not contain said introduced DNA.

29. (Amended) The plant of claim 28, wherein said storage organ contains a reduced level of squalene, cycloartenol, 24-methyl cycloartenol, obtusifoliol, stigmasta-7-enol, campesterol, or mixtures thereof, compared to a corresponding transgenic plant that comprises introduced DNA encoding a polypeptide having 3-hydroxy-3-methylglutaryl-Coenzyme A reductase enzyme activity but that does not contain introduced DNA encoding at least one polypeptide having squalene epoxidase enzyme activity.

a7

31. (Amended) A transformed seed of a plant according to any one of claims 24 to 30.

32. (Amended) Transgenic progeny of a plant according to any one of claims 24 to 30.

33. (Amended) A transformed plant cell or transformed plant cell of a plant according to any one of claims 24 to 30.

a8

35. (Amended) A transformed plant produced from a seed according to claim 31.

a9

67. (Amended) The transformed storage organ of claim 18, wherein said at least one transformed host cell further contains a recombinant vector comprising as operably linked components, a promoter, a DNA sequence encoding a tocopherol synthesis pathway enzyme and a transcription termination sequence.

68. (Amended) The transformed storage organ of claim 18, wherein said tocopherol synthesis enzyme is S-adenosylmethionine-dependent γ-tocopherol methyltransferase.

II. REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.111

A. Status of the Claims

Claims 1-77 were pending in the case at the time of the action. Applicants elected Group I claims, claims 1-35, 38, 40, 42 and 63-68 in response to a Restriction Requirement issued in the case. Claims 36, 37, 39, 41, 43-62 and 69-77 were cancelled herein as drawn to non-elected subject matter. The remaining claims have been amended pursuant to the election. Claims 1, 3, 6, 12, 14-20, 25-29, 31-33, 35, and 67-68 have been amended herein. Claims 1-35, 38, 40, 42 and 63-68 are now pending and presented for reconsideration.

B. Rejections Under 35 U.S.C. §112, First Paragraph – Written Description

The Action rejects claims 1-35, 38, 40, 42 and 63-68 under 35 U.S.C. § 112, first paragraph, as not being supported by an adequate written description in the specification. In particular, it is stated that a written description has not been provided for the full scope of sequences encoding polypeptides having the recited activities of HMG-CoA and squalene epoxidase.

Applicants first note that HMG-CoA reductase and squalene epoxidases were well known in the art at the time the application was filed. What was not known is that these sequences could be used together or that benefit would be achieved thereby. Applicants therefore need not describe these sequences given that they were known in the art, although Applicants have nonetheless done so. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). For example, set forth at pages 62-72 of the specification are numerous citations to known HMG-CoA reductases, as set forth below. For example, Chappell *et al.*, (U.S. Patent No. 5,349,126; incorporated by reference) describe the nucleotide sequence of the hamster and human gene for HMG-CoA

reductase. The structures and portions of two catalytically active segments of hamster HMG-CoA reductase were also previously defined (Liscum *et al., J. Biol. Chem.*, 260(1):522 (1985). Two genes encoding HMG-CoA reductase in yeast, designated, HMG1 and HMG2, were also disclosed in Chappell *et al.* and Basson *et al.* (*Mol. Cell Biol.*, 8(9):3797 (1988)). It was indicated that the entire HMG1 gene comprises about 3360 base pairs (SEQ ID NO:3 of Chappell *et al.*), and that the intact HMG-CoA reductase 1 comprises an amino acid sequence of about 1054 amino acid residues (SEQ ID NO:4 of Chappell *et al.*). The studies also indicated that the catalytic region of HMG-CoA reductase 1 comprises from about residue 618 to about reside 1054: i.e., the COOH-terminus; while the catalytic region comprises base pairs from about nucleotide position 1974 to about position 3282 of Fig. 3 of Chappell *et al.*

A nucleic acid sequence encoding HMG-CoA reductase from *Hevea brasiliensis* has also been described (Chye *et al.* (1991) *Plant Mol. Biol.* 16: 567-577); as has a nucleic acid sequence encoding an *Arabidopsis thaliana* HMG-CoA reductase (Caelles *et al.* (1989) *Plant Mol. Biol.* 13: 627-638; GenBank accession number L19261). U.S. Patents Nos. 5,306,862 and 5,365,017 disclose additional DNA sequences encoding HMG-CoA reductases.

Numerous further examples of HMG CoA-reductase sequences were described on Genbank and listed in the application at pages 68-72. A sampling of the sequences given includes those from: *Methanobacterium thermoautotrophicum*, *Sulfolobus solfataricus*, *Saccharomyces cerevisiae*, *Fusarium moniliforme* (gibberella fujikuroi), *Dictyostelium discoideum* (slime mold), *Oyza sativa* (rice), *Zea mays* (maize), *Hevea brasiliensis* (para rubber tree), *Catharanthus roseus* (rosy periwinkle; madagascar periwinkle), *Lycopersicon esculentum* (tomato), *Nicotiana sylvestris* (wood tobacco), *Solanum tuberosum* (Potato), *Raphanus sativus* (radish), *Arabidopsis thaliana*, *Cucumis melo*, *Camptotheca acuminata*, *Rattus norvegicus* (rat),

Oryctolagus cuniculus (rabbit), *Homo sapiens* (Human), and *Mus musculus* (Mouse), as well as sequences from other organisms.

Squalene epoxidase (also called squalene monooxygenase) was also well known and is fully described in the patent application, for example, at pages 62-65. As indicated, the enzyme reference number for squalene epoxidase was given in Enzyme Nomenclature 1992, p. 146. Among examples of squalene epoxidase cited in the application that were known in the art are *Arabidopsis* squalene epoxidase protein sequence Accession No. AC004786 (SEQ ID NO:1), *Arabidopsis* squalene epoxidase Accession No. N64916 (SEQ ID NO:2), *Arabidopsis* squalene epoxidase Accession No. T44667 (SEQ ID NO:3), *Arabidopsis* squalene epoxidase from clone ID ATA506263 disclosure SEQ ID NO:4, clone ID ATA304243 disclosure SEQ ID NO:6, clone ID ATA102071 disclosure SEQ ID NO: 8, clone ATA504158 disclosure SEQ ID NO:10, several homologues of *Arabidopsis* and Brassica squalene epoxidase genes reported by Schafer *et al.* ((1999) *Plant Mol. Biol.* 39(4): 721-728), and mammalian squalene epoxidase (Japanese patent application No. 07194381). Recombinant constructs encoding squalene epoxidase are also given in Figs. 30 and 31 of the specification.

Still other examples of squalene epoxidases were known as of the filing date. For example, squalene epoxidase from at least the following organisms was known: yeast (*Candida albicans*) (Favre B, Ryder NS. (1997) "Cloning and expression of squalene epoxidase from the pathogenic yeast," *Gene.* Apr 11;189(1):119-26), human (Laden, B.P., Tang,Y. and Porter, T.D (2000) "Cloning, heterologous expression, and enzymological characterization of human squalene monooxygenase," *Arch. Biochem. Biophys.* 374 (2), 381-388), mouse (Kosuga K, Hata S, Osumi T, Sakakibara J, Ono T., (1995) "Nucleotide sequence of a cDNA for mouse squalene epoxidase.," *Biochim Biophys Acta.* Feb 21;1260(3):345-8) and rat (Sakakibara J, Watanabe R,

Kanai Y, Ono T. (1995) "Molecular cloning and expression of rat squalene epoxidase." *J Biol Chem.* Jan 6;270(1):17-20). Similarly, in U.S. Pat. No. 6,153,815, issued November 28, 2000 and which is cited against Applicants in the 103 rejection, squalene epoxidase from the plant family *Brassicaceae* is said to be disclosed. Finally, with regard to S-adenosylmethionine-dependent γ-tocopherol methyltransferase, it is noted that these are disclosed and claimed in WO 00/61771, which was incorporated by reference in the current specification.

As indicated above, numerous representative HMG-CoA reductase and squalene epoxidase genes were known as of the filing date and were disclosed in the specification. Applicants were thus in possession of the sequences pursuant to 35 U.S.C. §112, first paragraph. As set forth in the Written Description Guidelines, written description must be reviewed from the perspective of one of skill in the art at the time the application is filed. Information that is well known in the art need not be described in detail in the specification, although Applicants have nonetheless done so here. It is therefore respectfully submitted that the written description requirement has been fully complied with. Removal of the rejection under 35 U.S.C. §112, first paragraph, is thus respectfully requested.

C. Rejections Under 35 U.S.C. §112, First Paragraph - Enablement

The Action rejects claims 1-35, 38, 40, 42 and 63-68 under 35 U.S.C. § 112, first paragraph, as not enabled for the claimed subject matter. In particular, it is stated that the application does not teach plants transformed with HMG-CoA reductase and squalene epoxidase, or any phenotypic effect thereof, particularly with respect to modification of the steroid biosynthetic pathway.

It is first noted that claims 1-7 are directed to recombinant constructs or vectors. The rejection with respect to phenotypic effects of heterologous expression are not applicable to these claims, as enablement must be viewed with respect to the claimed subject matter. Applicants fully describe the construction of recombinant vectors in the specification and no allegation to the contrary has been made. It is therefore believed that the rejection with respect to claims 1-7 is thus moot.

Similarly, claims 8-13 are directed to host cells transformed with a recombinant construct or vector. All that is required for enablement of these claims is that one of skill in the art be able to transform a host cell with the recited vector or recombinant construct. The Action does not state that transformation of plant cells is not taught by the application. Further, Examples 1-3 of the specification describe the introduction of recombinant constructs comprising HMG-CoA reductase in plant cells and creation of transgenic plants. This subject matter is thus also enabled and it is believed that the rejection is moot with respect to these claims as well.

Claims 14-19 are directed to transformed storage organs transformed with the aforementioned recombinant constructs. As set forth at page 96 of the application, storage organs are the "seeds, fruits or vegetable parts of a plant." Therefore transformed storage organs are produced by transforming a plant. Examples 1-3 describe the transformation of plants with recombinant constructs and therefore enable these claims. Claims 63-68 depend from and further narrow claims 8, 10 or 18, and are therefore fully enabled for the same reasons as the base claim pursuant to 37 C.F.R. §1.75(c).

It is only the remaining claims that involve phenotypic expression as recited in the Action. Enablement for these claims is provided in the working examples. In particular, the increase of both overall sterol biosynthesis and steroid precursors is demonstrated in Examples

1-3 of the application. Heterologous expression of rubber and *Arabidopsis* HMG-CoA reductase driven by seed-specific promoters in transgenic canola and soybean was in particular shown to result in sterol over-production up to 2-4 fold higher in seeds from these transgenic plants (see Examples 1-2). A higher accumulation of pathway intermediates in soybean than canola was also shown.

As described in the examples, the majority of transgenic soybean lines harboring the recombinant binary vector pMON43057, comprising a cDNA fragment encoding the catalytic domain of *Arabidopsis* HMGR1, showed 3 to 5-fold increase in total sterols. The best performing transgenic lines, GM_A13342 and GM_A13634, showed 6.5- and 6.1-fold increase in total sterols, respectively. These lines showed 2- to 2.6-fold increase in sitosterol, 1.5 to 2.2-fold increase in sitostanol and no significant change in the campesterol levels. Hence the major proportion of the total sterol increase was shown to be accounted by the accumulation of pathway intermediates, which include squalene, cycloartenol, 24-methylene cycloartenol, obtusifoliol, isofucosterol, and stigmasta-7-enol.

The best performing transgenic soybean lines, GM_A13342 and GM_A13634, showed a 32.6- and 32.2-fold increase in pathway intermediates accumulation, respectively, as compared to a control. In all the transgenic lines harboring the pMON43057 vector, 50-70% of the total increase was accounted by the increase in the pathway intermediates accumulation as compared to the control. The pathway intermediates include squalene, cycloartenol, 24-methylene cycloartenol, obtusifoliol, isofucosterol, and stigmasta-7-enol. The results demonstrated enablement for the modification of sterol biosynthesis precursors.

The inventors also demonstrated the ability to express HMG-CoA reductase in combination with a steroid biosynthesis gene. In particular, heterologous expression of HMG-

CoA reductase and sterol methyl transferase II (SMTII) was demonstrated with the construct pMON43058 (Figure 10), carrying both the catalytic domain of *Arabidopsis* HMGR1 and *Arabidopsis* SMTII, and was introduced into soybeans to yield modification of sterol biosynthesis. As shown in Example 3 and Table 4, six transgenic lines harboring pMON43058 produced 5.8- to 6-fold increase in total sterols, and the rest of 10 transgenic lines with the pMON43058 showed 3- to 5-fold increase in total sterols. The best performing transgenic lines showed about 2- to 3-fold increase in sitosterol and 4.5- to 6-fold increase in sitostanol levels, with a reduction in campesterol accumulation by 50% in these lines. The latter reduction was due to overexpression of the *Arabidopsis* SMTII enzyme, which enhances the carbon flux towards the synthesis of 24-ethyl sterols, thereby reducing the carbon flux through the pathway leading to the synthesis of 24-methyl sterols. The results demonstrated the ability to selectively modify sterol biosynthesis and accumulation steroid biosynthesis precursors.

The inventors also showed, surprisingly, that in soybean seeds expressing HMG-CoA reductase, squalene accumulates to a very high level, ~3mg/g seed, which is approximately 100-fold higher than in nontransgenic controls (see specification at pages 32-33). This surprising result showed, for the first time, that squalene epoxidase represents a "bottleneck" in the further conversion of the steroid precursor squalene for sterol production in soybeans. Combined with the results set forth above, the ability was demonstrated to increase overall sterol content as well as steroid pathway precursors. Applicants therefore submit that the claims are fully enabled by the specification. Removal of the rejection under 35 U.S.C. §112, first paragraph is thus respectfully requested.

D. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 14-15, 20, 25 and 26 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicant regards as the invention.

(1) The Action rejects claims 14 and 15 as being in improper independent form. In response it is noted that the claim has been amended as suggested. Removal of the rejection is thus requested.

(2) Claim 20 is rejected as not having antecedent basis for "regenerating said transformed plant cell." In response, it is noted that the claim has been amended to correct the antecedent basis. Removal of the rejection is thus respectfully requested.

(3) Claim 25 is rejected for use of the term "a non-transformed plant of the same strain" as not reflecting art accepted language regarding plants. In response it is noted that the claim has been amended to clarify the language. Removal of the rejection is thus respectfully requested.

(4) The Action rejects claim 26 as being indefinite in that it is not clear how a plant could have increased sterol levels and have further limitations that would reduce the level of squalene or downstream sterol products. In response, Applicants note that the added limitation referred to specifies particular downstream sterol precursors and not overall sterol content. As was indicated above, Applicants have shown that heterologous expression of steroid biosynthetic pathway genes in combination with an HMG-CoA reductase gene may be used to increase flux through a given step in the pathway. In this manner, the level of the upstream precursor at the step is decreased, but overall sterol content increased. It is thus respectfully submitted that the claim is definite. Removal of the rejection is therefore respectfully requested.

E. Rejection Under 35 U.S.C. §101

The Action has rejected claims 15, 17-19, 31-35 and 67-68 under 35 U.S.C. §101 as being directed to non-statutory subject matter for encompassing non-transgenic plants. In response, Applicants note that claims 15, 17-19, 31-33, 35 and 67-68 have been amended to clarify that they are directed to transformed or transgenic compositions and not products of nature per se. With regard to claim 34, Applicants note that this is directed to a cell culture that comprises transgenic cells and is therefore directed to statutory subject matter not embracing products of nature.

F. Rejections Under 35 U.S.C. §103(a)

The Action rejects claims 1-35, 38, 40 and 42 under 35 U.S.C. §103 as being obvious over Chappell *et al.* (U.S. Patent No. 5,589,619) in view of Covello *et al.* (U.S. Patent No. 6,153,815). In particular, it is stated that Chappell *et al.* teaches increased squalene and total sterol accumulation in transgenic tobacco plants and storage organs by expression of HMG-CoA reductase with a lectin promoter. It is acknowledged that Chappell does not teach expression of downstream sterol biosynthetic enzymes, such as squalene epoxidase, but it is stated that this would be obvious in view of Covello *et al.* teaching a *B. napus* transgenic cDNA encoding squalene epoxidase in antisense orientation and a resulting increase in squalene accumulation in *Arabidopsis* transformed with this construct.

Applicants note that the references do not teach all elements of the claims. Specifically, the references do not teach expression of a sequence encoding squalene epoxidase enzyme activity or constructs therefore. For example, Covello notes in the Abstract that in the method of the invention "DNA is introduced into the genome in a way that results in *down-regulation* of an

exogenous plant squalene gene to *suppress* the expression of squalene epoxidase" (emphasis added). The Action acknowledges that this element is not taught by Chappell *et al.* It is thus respectfully submitted that all elements of the claims are not in the prior art and thus the claims are not rendered obvious.

Applicants further note that Covello expressly teaches away from the invention. The current invention relates to nucleic acids comprising sequences that encode squalene epoxidase enzyme activity and uses thereof, whereas Covello teaches that it is beneficial to specifically suppress such activity. This is explained at the very beginning of the Detailed Description of the Invention section of Covello in the "General Discussion" where it is stated that:

> The concept underlying the present invention is to identify squalene epoxidase genes of oilseed plants (or possibly other plants, since all plants appear to have genes for the production of squalene, and particularly those plants that are capable of accumulating squalene in their harvestable tissue) and then to use that knowledge to create genetically-modified plants in which the *expression of squalene expoxidase is decreased* partially or fully compared to the natural level of expression, so that *squalene naturally produced by the plants can accumulate* in the seeds or other tissue to levels that make extraction commercially attractive. (emphasis added)

As such, Covello teaches away from the invention. Covello teaches that benefit is gained by *decreasing* squalene epoxidase activity in a plant, not increasing it. One of skill in the art reading Covello would have an express motivation to *not* carry out the claimed invention, otherwise the entire purpose of the Covello technique would not be achieved. In contrast, the claimed invention relates to increasing squalene epoxidase. There was, therefore, no "common knowledge in the art that transformation vectors comprising cDNA encoding a downstream enzyme of the squalene sterol biosynthetic pathway" are valuable for increasing total sterol levels. Covello indicates that squalene epoxidase must be down-regulated to achieve benefit. Where references taken in combination would produce a "seemingly inoperative device," they are not combinable and cannot serve as predicates for a *prima facie* case of obviousness. *In re*

Gordon, 733 F.2d 900, 902 (Fed. Cir. 1984). Therefore, in addition to not providing all elements of the claims, the references are not properly combinable and teach away from the invention.

Removal of the rejection under 35 U.S.C. §103 is thus respectfully requested.

G. **Conclusion**

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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